STN-Structure Search 8-9-05

10/695,644

=> d ibib abs hitstr 1-197

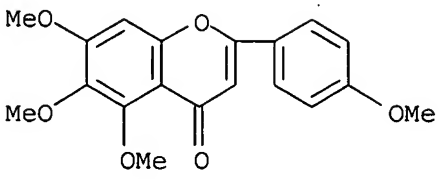
L6 ANSWER 1 OF 197 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:255972 CAPLUS
DOCUMENT NUMBER: 142:423446
TITLE: Involvement of nitric oxide in both central and peripheral haemodynamic effect of D/L-nebivolol and its enantiomers in rats
AUTHOR(S): Sacco, Giuseppe; Evangelista, Stefano; Criscuoli, Marco; Goso, Cristina; Bigioni, Mario; Binaschi, Monica; Manzini, Stefano; Maggi, Carlo Alberto
CORPORATE SOURCE: Pharmacology, Menarini Ricerche spa, Rome, 00040, Italy
SOURCE: European Journal of Pharmacology (2005), 511(2-3), 167-174
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The cardiovascular profile of the racemate D/L-nebivolol and its enantiomers administered by i.v. or by intracerebroventricular (i.c.v.) route was investigated in anesthetized normotensive rats. D/L-Nebivolol (0.1-0.5 mg/kg) induced a dose-related reduction in blood pressure when administered by i.c.v. route. These hypotensive effects were more marked as compared to those achieved by peripheral administration of D/L-nebivolol (0.1-1 mg/kg i.v.). Both enantiomers contributed to the hypotensive effect of D/L-nebivolol by i.c.v. route, while the effects of the drug on blood pressure by i.v. route were due to the D-enantiomer. The bradycardic effect of the racemic form given i.v. was dose-related and, at the highest dose (1 mg/kg), was more pronounced as compared to i.c.v. route. D-Nebivolol was responsible for chronotropic effects by both the i.v. and i.c.v. route, although by i.c.v. route L-nebivolol also induced a reduction in heart rate. The nitric oxide synthase inhibitor N ω-nitro-L-arginine Me ester (L-NAME) administered at 5 mg/kg i.v. bolus+0.1 mg/kg/min infusion or at 2.5 mg/kg i.c.v. counteracted the effects of D/L-nebivolol (either 1 mg/kg i.v. or 0.5 mg/kg i.c.v.) on blood pressure, while it did not inhibit the cardiovascular changes induced by isoprenaline (300 ng/kg i.v.) or calcitonin gene-related peptide (CGRP; 400 ng/kg i.v.). In addition, i.c.v. effects of D/L-nebivolol on blood pressure and heart rate were not affected by pre-treatment with atropine (2 mg/kg i.v.). The present findings demonstrate that D/L-nebivolol produced haemodynamic changes following both peripheral and central administration; these latter findings are mainly due to its L-enantiomer and these effects involve the L-arginine/nitric oxide pathway.

IT **118457-14-0**, dl-Nebivolol **118457-15-1**, d-Nebivolol **118457-16-2**, l-Nebivolol
RL: PAC (Pharmacological activity); BIOL (Biological study)
(involvement of nitric oxide in both central and peripheral haemodynamic effect of D/L-nebivolol and its enantiomers in rats)

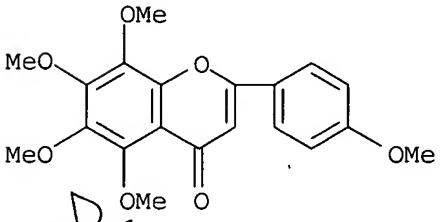
RN 118457-14-0 CAPLUS
CN 2H-1-Benzopyran-2-methanol, α,α'-[iminobis(methylene)]bis[6-fluoro-3,4-dihydro-, (αR,α'R,2R,2'S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



CM 5

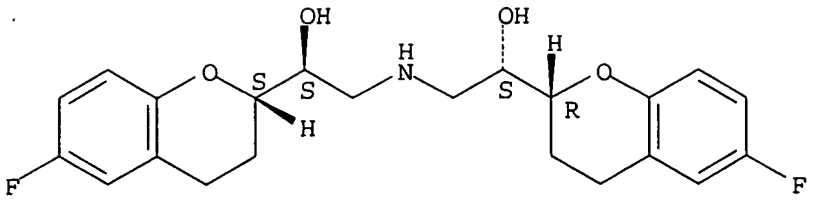
CRN 481-53-8
CMF C20 H20 O7



Inventor 5

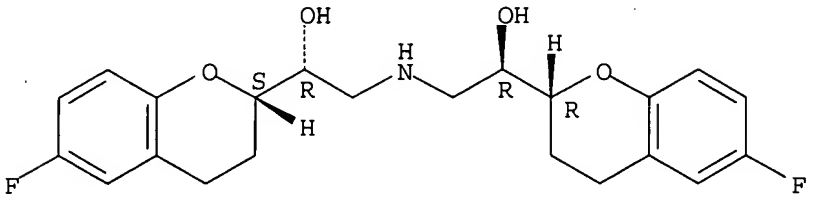
L6 ANSWER 69 OF 197 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:849381 CAPLUS
DOCUMENT NUMBER: 137:333153
TITLE: Nitrosated and nitrosylated nebivolol and its metabolites, compositions and methods of use
INVENTOR(S): Garvey, David S.
PATENT ASSIGNEE(S): Nitromed, Inc., USA
SOURCE: PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002087508	A2	20021107	WO 2002-US13667	20020501
WO 2002087508	A3	20031211		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2446064	AA	20021107	CA 2002-2446064	20020501
EP 1406608	A2	20040414	EP 2002-766876	20020501
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004528337	T2	20040916	JP 2002-584860	20020501
US 2004132805	A1	20040708	US 2003-695644	20031029
PRIORITY APPLN. INFO.:			US 2001-287725P	P 20010502
			WO 2002-US13667	W 20020501



RN 118457-15-1 CAPLUS
CN 2H-1-Benzopyran-2-methanol, α,α'-[iminobis(methylene)]bis[6-fluoro-3,4-dihydro-, (αR,α'R,2R,2'S)- (9CI) (CA INDEX NAME)

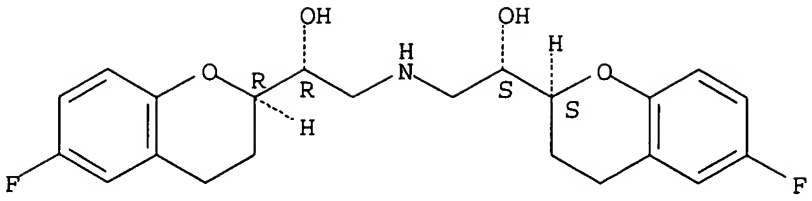
Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

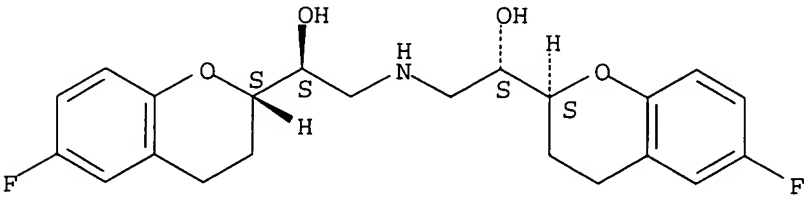
L6 ANSWER 115 OF 197 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:137173 CAPLUS
DOCUMENT NUMBER: 134:178396
TITLE: Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction
INVENTOR(S): Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001012584	A2	20010222	WO 2000-EP7225	20000727
WO 2001012584	A3	20020829		
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2381409	AA	20010222	CA 2000-2381409	20000727
BR 2000013264	A	20020416	BR 2000-13264	20000727
EP 1252133	A2	20021030	EP 2000-953102	20000727
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003515526	T2	20030507	JP 2001-516885	20000727
NZ 516889	A	20041029	NZ 2000-516889	20000727
ZA 2002000628	A	20030423	ZA 2002-628	20020123



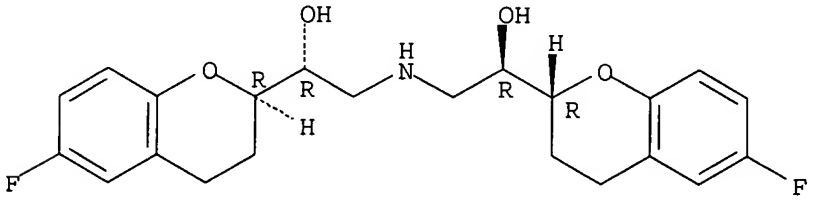
RN 119365-28-5 CAPLUS
CN 2H-1-Benzopyran-2-methanol, α,α'-[iminobis(methylene)]bis[6-fluoro-3,4-dihydro-, [2S-[2R*[R*[R*(R*)]]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



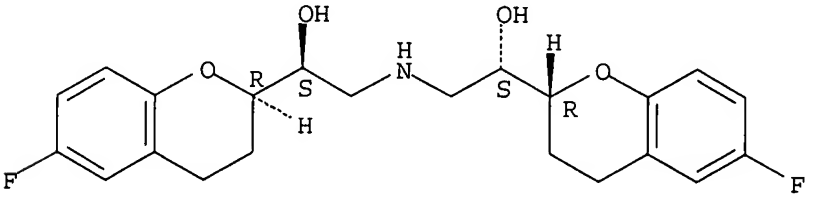
RN 119365-29-6 CAPLUS
CN 2H-1-Benzopyran-2-methanol, α,α'-[iminobis(methylene)]bis[6-fluoro-3,4-dihydro-, [2R-[2R*[R*[R*(R*)]]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



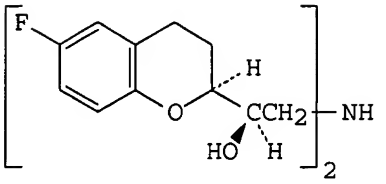
RN 119365-30-9 CAPLUS
CN 2H-1-Benzopyran-2-methanol, α,α'-[iminobis(methylene)]bis[6-fluoro-3,4-dihydro-, [2R-[2R*[S*[S*(R*)]]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 194 OF 197 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:50943 CAPLUS
DOCUMENT NUMBER: 110:50943
TITLE: Cardiovascular effects of dl-nebivolol and its enantiomers - a comparison with those of atenolol
AUTHOR(S): Van de Water, A.; Xhonneux, R.; Reneman, R. S.;

Janssen, P. A. J.
CORPORATE SOURCE: Cardiovasc. Dep., Janssen Res. Found., Beerse, Belg.
SOURCE: European Journal of Pharmacology (1988), 156(1), 95-103
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



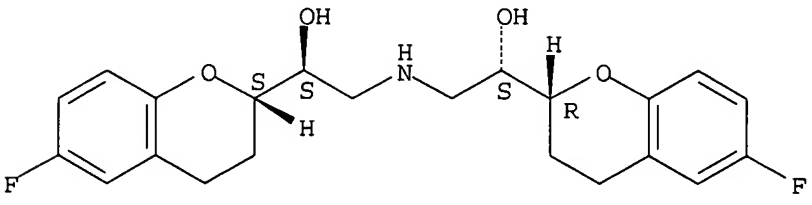
I

AB The cardiovascular effects of dl-nebivolol (I) and its enantiomers d-nebivolol and l-nebivolol were studied in closed-chest anesthetized dogs, with atenolol as a reference substance. In vitro d-nebivolol is a β1-adrenoceptor antagonist and l-nebivolol is devoid of β-adrenoceptor-blocking properties. Unlike atenolol, dl-nebivolol did not depress left ventricular function and slightly reduced peripheral vascular resistance over the dose range 0.0025-0.34 mg/kg, i.v. These observations are likely to be clin. relevant because one daily oral dose of 5 mg dl-nebivolol effectively lowers arterial blood pressure in patients with hypertension. The favorable hemodynamic profile of dl-nebivolol can be ascribed to the l-enantiomer because the cardiovascular effects of this enantiomer are similar to those of the racemate. The cardiovascular profile of the d-enantiomer is similar to that of atenolol but its depressant effect on left ventricular function occurs at higher doses.

IT **118457-14-0 118457-15-1 118457-16-2**
RL: PRP (Properties)
(cardiovascular effects of, enantiomer in relation to)

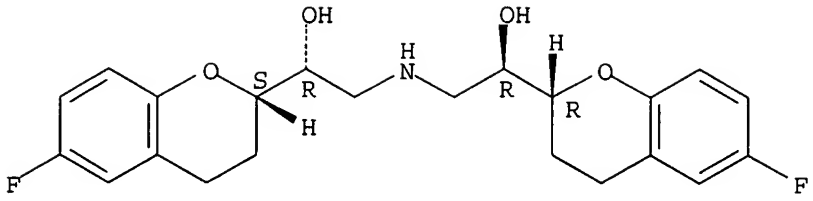
RN 118457-14-0 CAPLUS
CN 2H-1-Benzopyran-2-methanol, α,α'-[iminobis(methylene)]bis[6-fluoro-3,4-dihydro-, (αR,α'R,2R,2'S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



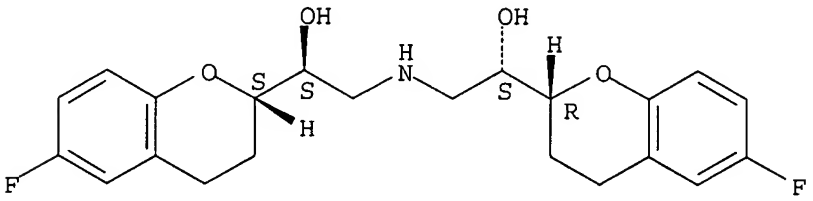
RN 118457-15-1 CAPLUS
CN 2H-1-Benzopyran-2-methanol, α,α'-[iminobis(methylene)]bis[6-fluoro-3,4-dihydro-, (αR,α'R,2R,2'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

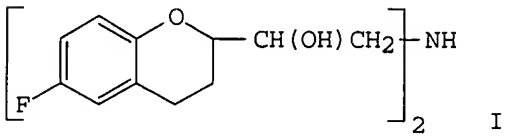


RN 118457-16-2 CAPLUS
CN 2H-1-Benzopyran-2-methanol, α,α'-[iminobis(methylene)]bis[6-fluoro-3,4-dihydro-, (αS,α'S,2R,2'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 195 OF 197 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:416771 CAPLUS
DOCUMENT NUMBER: 109:16771
TITLE: Pharmacological and hemodynamic profile of nebivolol, a chemically novel, potent, and selective β1-adrenergic antagonist
AUTHOR(S): Van de Water, A.; Janssens, W.; Van Neuten, J.; Xhonneux, R.; De Cree, J.; Verhaegen, H.; Reneman, R. S.; Janssen, P. A. J.
CORPORATE SOURCE: Res. Lab., Janssen Pharm., Beerse, B-2340, Neth.
SOURCE: Journal of Cardiovascular Pharmacology (1988), 11(5), 552-63
CODEN: JCPCDT; ISSN: 0160-2446
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The pharmacol. profile of nebivolol (N)(I), a chemical novel β-adrenergic antagonist, was assessed in isolated tissues, awake spontaneously hypertensive rats (SHR), closed-chest anesthetized dogs, and humans. In vitro, N was a potent antagonist of β1-adrenergic receptors and only a weak β2-adrenergic antagonist. The selectivity for the β1-adrenergic receptor was higher for N than for any of the reference compds. In dogs-similarly with atenolol-N was more potent in blocking the isoprenaline (I)-induced increases in left ventricular performance than the I-induced decrease in arterial pressure. In dogs, as compared with propranolol, N (0.025 and 0.01 mg.kg-1 i.v.) increased

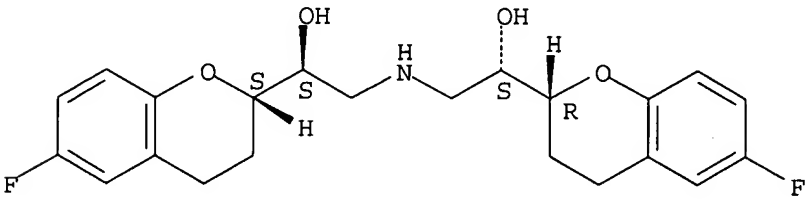
cardiac output and stroke volume, lowered systemic vascular resistance, and had no significant effect on the variables related to left ventricular contraction. In contrast to other β-adrenergic antagonists, N acutely lowered arterial blood pressure in SHR (1.,25 mg.kg-1 i.p.) and in hypertensive patients (1 oral dose of 5 mg) for several hours. In healthy human volunteers, N (5 mg) lowered systemic vascular resistance during daily oral treatment and did not neg. affect left ventricular function. In conclusion, N is a potent and selective β1-adrenergic blocking agent with an interesting hemodynamic profile. In hypertensive subjects and SHR, a single dose lowers arterial blood pressure for substantial periods of time.

IT **118457-14-0**, Nebivolol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cardiovascular system response to, as β1-adrenergic antagonist, in humans and laboratory animals)

RN 118457-14-0 CAPLUS

CN 2H-1-Benzopyran-2-methanol, α,α'-[iminobis(methylene)]bis[6-fluoro-3,4-dihydro-, (αR,α'R,2R,2'S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L6 ANSWER 196 OF 197 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1986:545898 CAPLUS

DOCUMENT NUMBER: 105:145898

TITLE: Hemodynamic effects in man during exercise of a single oral dose of narbivolol (R 67555), a new beta-1-adrenoceptor blocking agent: a comparative study with atenolol, pindolol, and propranolol

AUTHOR(S): De Cree, Jean; Geukens, Hedwig; Leempoels, Jos; Verhaegen, Herman

CORPORATE SOURCE: Dep. Clin. Pharmacol., Janssen Pharm. Res. Lab., Beerse, B-2340, Belg.

SOURCE: Drug Development Research (1986), 8(1-4), 109-17
CODEN: DDREDK; ISSN: 0272-4391

DOCUMENT TYPE: Journal

LANGUAGE: English

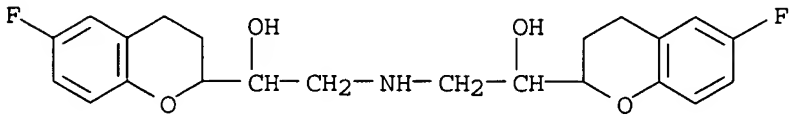
AB In 8 normal volunteers, R 67555 at 5 and 10 mg lowered the exercise-induced increase of systolic blood pressure by 20 and 25%, and the exercise-induced increase of heart rate by 20 and 21% resp. The blood pressure lowering effect of R 67555 6 h after intake was comparable to that observed after atenolol, pindolol, and propranolol. In contrast, the lowering of exercise-induced increase of heart rate was less with R 67555 than with the other β-blockers tested. The ratio of PEP-LVET (left ventricular ejection time), a measure of left ventricular performance, was increased 3 h after intake of atenolol, propranolol, and 10 mg of R 67555 but not after pindolol and 5 mg of R 67555. Six h after administration of pindolol and of 5 mg of R 67555, the ratio PEP/LVET was lowered as compared with control values. The post-exercise LVET was shortened 3 and 6 h after intake of 5 and 10 mg of R 67555, whereas a trend to prolongation was observed after administration of atenolol, pindolol, and

propranolol.

IT **99200-09-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cardiovascular system response to, in exercise, in humans)

RN 99200-09-6 CAPLUS

CN 2H-1-Benzopyran-2-methanol, α,α'-[iminobis(methylene)]bis[6-fluoro-3,4-dihydro- (9CI) (CA INDEX NAME)



L6 ANSWER 197 OF 197 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1986:5773 CAPLUS

DOCUMENT NUMBER: 104:5773

TITLE: 2,2'-Iminobisethanol derivatives

INVENTOR(S): Van Lommen, Guy Rosalia Eugene; De Bruyn, Marcel Frans Leopold; Schroven, Marc Francis Josephine

PATENT ASSIGNEE(S): Janssen Pharmaceutica N. V., Belg.

SOURCE: Eur. Pat. Appl., 49 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

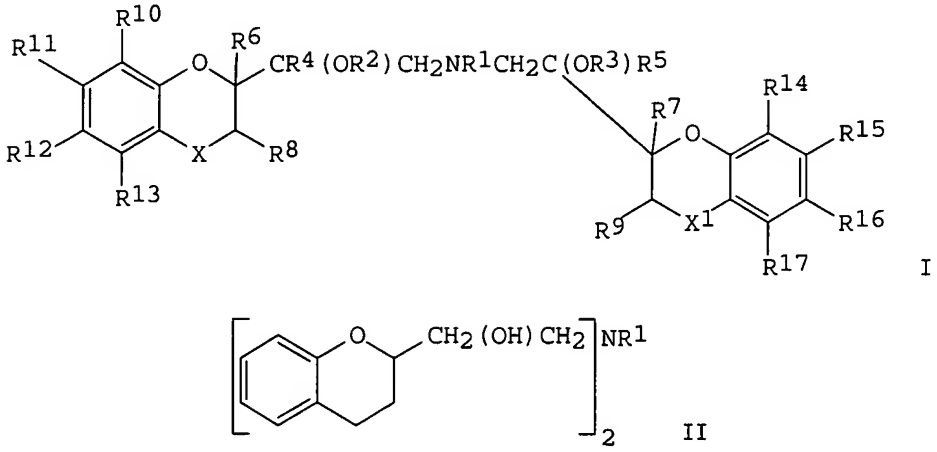
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 145067	A2	19850619	EP 1984-201693	19841122
EP 145067	A3	19860326		
EP 145067	B1	19890125		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 4654362	A	19870331	US 1984-660355	19841012
CA 1337429	A1	19951024	CA 1984-468108	19841119
PL 146342	B1	19890131	PL 1984-250524	19841121
AT 40361	E	19890215	AT 1984-201693	19841122
JP 60132977	A2	19850716	JP 1984-252038	19841130
JP 02050114	B4	19901101		
DD 235453	A5	19860507	DD 1984-270216	19841203
RO 91184	B3	19870730	RO 1984-116496	19841203
IL 73706	A1	19880731	IL 1984-73706	19841203
DK 8405770	A	19850606	DK 1984-5770	19841204
DK 165112	B	19921012		
DK 165112	C	19930301		
FI 8404777	A	19850606	FI 1984-4777	19841204
FI 82460	B	19901130		
FI 82460	C	19910311		
NO 8404845	A	19850606	NO 1984-4845	19841204
NO 169839	B	19920504		
NO 169839	C	19920812		
HU 37418	A2	19851228	HU 1984-4482	19841204
HU 202219	B	19910228		
ES 538256	A1	19860101	ES 1984-538256	19841204
ZA 8409445	A	19860730	ZA 1984-9445	19841204
CS 250242	B2	19870416	CS 1984-9320	19841204
SU 1428199	A3	19880930	SU 1984-3826501	19841204
AU 8436326	A1	19850613	AU 1984-36326	19841205

AU 573658	B2	19880616			
DK 9200118	A	19920131	DK 1992-118		19920131
DK 165321	B	19921109			
DK 165321	C	19930329			
PRIORITY APPLN. INFO.:			US 1983-558081	A	19831205
			EP 1984-201693	A	19841122

GI



I

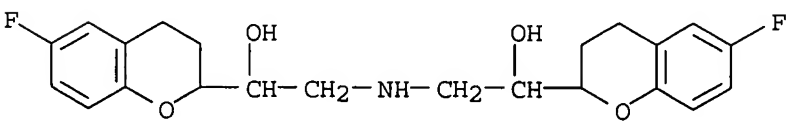
II

AB Iminobis(benzopyranyl and related compds. I [R1 = H, (un)substituted alkyl, aryl, acyl; R2, R3 = H, acyl; R4-R9 = H, alkyl; R10-R17 = H, halo, alkyl, alkenyl, alkoxy, alkylthio, OH, amino, etc.; X, X1 = bond, CH2, CO, CS, CH(OH), CH(O2CR18); R18 = alkyl], useful as β-adrenergic receptor blockers, were prepared Thus, 3,4-dihydro-2-oxiranyl-2H-1-benzopyran reacted with PhCH2NH2 to give 8% iminobis(benzopyran) compds. II (R1 = CH2Ph). An oral drop formulation (50 L) contained II 500 g, 2-hydroxypropanoic acid 0.5 L, Na saccharin 1750 g, cocoa flavor 2.5 L, purified H2O 2.5 L, and polyethylene glycol to 50 L. II (R1 = H) was active as a β-adrenergic receptor blocker in vitro.

IT **99200-09-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as β-sympatholytic)

RN 99200-09-6 CAPLUS

CN 2H-1-Benzopyran-2-methanol, α,α'-[iminobis(methylene)]bis[6-fluoro-3,4-dihydro- (9CI) (CA INDEX NAME)



=> d his

(FILE 'HOME' ENTERED AT 11:30:09 ON 09 JUN 2005)

FILE 'REGISTRY' ENTERED AT 11:30:31 ON 09 JUN 2005

L1 STRUCTURE UPLOADED

L2 0 S L1

L3 STRUCTURE UPLOADED

```
L4             2 S L3
L5            31 S L3 FULL

     FILE 'CAPLUS' ENTERED AT 11:32:13 ON 09 JUN 2005
L6           197 S L5

=> d l3
L3 HAS NO ANSWERS
L3                STR
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.


=>
```

=> d ibib abs hitstr

L1 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:849381 CAPLUS
DOCUMENT NUMBER: 137:333153
TITLE: Nitrosated and **nitrosylated** **nebivolol** and its metabolites, compositions and methods of use
INVENTOR(S): Garvey, David S.
PATENT ASSIGNEE(S): Nitromed, Inc., USA
SOURCE: PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002087508	A2	20021107	WO 2002-US13667	20020501
WO 2002087508	A3	20031211		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2446064	AA	20021107	CA 2002-2446064	20020501
EP 1406608	A2	20040414	EP 2002-766876	20020501
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004528337	T2	20040916	JP 2002-584860	20020501
US 2004132805	A1	20040708	US 2003-695644	20031029
PRIORITY APPLN. INFO.:			US 2001-287725P P	20010502
			WO 2002-US13667 W	20020501

OTHER SOURCE(S): MARPAT 137:333153

AB Compns. comprising nitrosated and/or nitrosylated derivs. of nebivolol or its metabolites, and optionally, a nitric oxide donor, an antioxidant, a cardiovascular agent, and/or a nitrosated compound used to treat cardiovascular diseases are described. The compds. and compns. of the invention can also be bound to a matrix. The nitric oxide donor used is a compound that donates, transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase and may preferably be isosorbide dinitrate and/or isosorbide mononitrate. The antioxidant may preferably be a hydralazine compound or a pharmaceutically acceptable salt thereof. The invention also provides methods for treating and/or preventing cardiovascular diseases characterized by nitric oxide insufficiency and for treating and/or preventing Raynaud's syndrome.

=> d his

(FILE 'HOME' ENTERED AT 16:43:15 ON 09 JUN 2005)

FILE 'CAPLUS' ENTERED AT 16:43:26 ON 09 JUN 2005
L1 1 S NITROSATED NEBIVOLOL OR NITROSYLATED NEBIVOLOL